

* * * * *

=> s boro pro or boro(W) (pro or prolin##)
3 BOBOPRO
1234 BOPO
14806 PPO
7342 PROLIN##
1 BOPO(W) (PRO OR PROLIN##)
L1 3 BOBOPRO OR BOPO(W) (PRO OR PROLIN##)
=> d t1,fa,date,kwic 1-3

US PAT NO: 5,288,707 [IMAGE AVAILABLE] L1: 2 of 3
TITLE: Borolysine peptidomimetics
DATE FILED: Jan. 29, 1993

TITLE: Borolysine peptidomimetics
US PAT NO: 5,288,707 [IMAGE AVAILABLE] DATE ISSUED: Feb. 22, 1994
APPL-NO: 08/011,443 DATE FILED: Jan. 29, 1993
FEN-PEL NO: 9017694 FRN FILED: Aug. 13, 1990
FEN-PEL CO: United Kingdom
FEL-US-DATA: Continuation of Ser. No. 743,847, Aug. 12, 1991,
abandoned.

SUMMARY:

PSUM(69)

BoroPro=analog of proline in which the --COOH

DETEDESC:

DETD(63)

Boc-D-TMS-al-Adgly-**boroPro**-OPin

DETEDESC:

DETD(63)

C. Boc-D-TMSal-Adgly-**boroPro**-OPin

DETEDESC:

DETD(69)

The . . . HCl, cyclizes to the boroproline derivative, which reacts
then with the active ester of step E to give the unexpected
Boc-D-TMSal-Adgly-**boroPro**-OPin as the major product. Flash
chromatography (2:1 hexane/EtOAc) of the crude product yields the title
compound (0.48 g) as a white foam, which is further purified by
recrystallization from ether/hexane to give the desired product
Boc-D-TMSal-Adgly-**boroPro**-OPin as a white crystalline compound.

US PAT NO: 4,935,493 [IMAGE AVAILABLE] L1: 3 of 3
TITLE: Protease inhibitors
DATE FILED: Oct. 6, 1987

DETD(21)

General . . . those skilled in the art of peptide synthesis. One exception is that in the preparation of a compound with the Pro-Thr-****boroPro**** sequence. Removal of acid labile protecting groups from threonine hydroxyl group results in a complex mixture of products. Thus, the . . .

DETD(22)

DETD(23)

The . . . 5 minutes, this mixture and one equivalent of triethylamine (or other sterically hindered base) are added to a solution of H-****boroPro****-pinacol dissolved in either cold chloroform or tetrahydrofuran.

DETD(24)

DETD(25)

Preparation of boroProline-pinacol (H-****boroPro****-pinacol)

DETD(26)

DETD(27)

Preparation of Boc-Ala-Pro-****boroPro****-pinacol

DETD(28)

DETD(29)

Boc-Ala-Pro-****boroPro****-pinacol was prepared by coupling Boc-Ala-Pro-OH to H-****boroPro****-pinacol. First, the dipeptide, Boc-Ala-Pro-OBzl, was prepared by the mixed anhydride procedure. Boc-Ala-OH (10 g, 52.8 mmoles) was reacted with N-methylmorpholine. . . .

DETD(30)

DETD(31)

Boc-Ala-Pro-OH (1.26 g, 4.28 mmoles) was coupled to H-****boroPro****-pinacol by the general procedure described for the preparation of Boc-Ala-Pro-OBzl. Boc-Ala-Pro-OH (1.26 g, 4.28 mmoles) was dissolved in 11 ml. . . . of cold THF and triethylamine (0.597 ml, 4.28 mmoles) were added and the mixture added to a cold solution of H-****boroPro****-pinacol.HCl (1.0 g, 4.28 mmoles) in 5 ml chloroform. After dissolving the reaction product in ethyl acetate and washing with aqueous. . . .

DETD(32)

DETD(33)

Preparation of H-Ala-Pro-****boroPro****-pinacol.HCl

DETD(34)

DETD(35)

DETD(36)

Preparation of Ac-Ala-Pro-***boroPro**-pinacol

DEDESC:

DETD(44)

H-Ala-Pro-***boroPro**-pinacol.HCL (0.22 g, 0.55 mmoles) was dissolved in 1 ml of THF and cooled to 0.degree. C. Acetic anhydride (0.078 ml, . . .

DEDESC:

DETD(46)

Preparation of MeOSuc-Ala-Ala-Pro-***boroPro**-pinacol.

DEDESC:

DETD(47)

MeOSuc-Ala-Ala-Pro-OH . . . procedure described in Kettner et al., J. Biol. Chem., 259: 15106-15114 (1984). MeOSuc-Ala-Ala-Pro-OH (1.59 g, 4.28 mmoles) was coupled to H-***boroPro** pinacol.HCl (1.00 g, 4.28 mmoles) by the mixed anhydride procedure described for the preparation of Boc-Ala-Pro-***boroPro**-pinacol except that, after filtration and evaporation of the reaction solvent, it was applied to a 2 cm column containing 10. . .

DEDESC:

DETD(49)

Preparation of Boc-Pro-Thr(OBzl)-***boroPro**-pinacol.

DEDESC:

DETD(51)

Boc-Pro-Thr(OBzl)-***boroPro**-pinacol was prepared by coupling Boc-Pro-Thr(OBzl)-OH (2.70 g, 6.42 mmoles) to H-***boroPro**-pinacol.HCL(1.50 g, 6.42 mmoles) using the procedure described for Boc-Ala-Pro-***boroPro**-pinacol. The product (2.4 g) was purified by chromatography on a 2.5.times.50 cm column of LH-20 in methanol and was obtained. . .

DEDESC:

DETD(53)

Preparation of Boc-Pro-Thr-***boroPro**-Pinacol

DEDESC:

DETD(54)

Boc-Pro-Thr-***boroPro**-pinacol was prepared by hydrogenation of Boc-Pro-Thr(OBzl)-***boroPro**-pinacol (from Example 6, 0.585 g, 0.79 mmoles). The protected peptide was dissolved in 100 ml of methanol and was hydrogenated. . .

-> log hold

DETD(55) (continued)